REMARKS

The Invention

The present invention relates to antibodies which specifically bind to an antigenic molecule from an isolated human herpes virus, wherein the antibodies do not specifically bind to an antigenic molecule from Epstein-Barr virus, human cytomegalovirus (CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri; and methods of detecting such antibodies in a biological sample. The isolated human herpes virus has the morphology of a human herpes virus and a double-stranded DNA genome of about 170 Kb and genomic DNA from the isolated human herpes virus hybridizes under stringent conditions with nucleic acid of molecular clone ZVH14 (ATCC Accession No. 40,247).

Status of the Claims

Applicants wish to thank Examiner Salimi for extending the courtesy of the telephonic discussion held on January 13, 2003 with Applicants' representative Carol Fang. During this interview, the nature of the reissue declaration was discussed. Applicants thank Examiner Salimi for his time.

Claims 1, 2, and 4-12 are pending. Applicants have amended claims 1, 2, 4, and 12. The amendments do not introduce new matter or raise new issues that would require further consideration and/or search. In particular, claims 1 and 4 have been amended to clarify the characteristics of the herpes virus to which the antibody specifically binds. In addition, claim 1 has been amended to ensure correct antecedent basis for "genomic DNA." Support for these amendments is found in claim 1 as filed and in the specification at, *e.g.*, col. 1, lines 44-45, col. 2, line 58; and col. 6, lines 3-16. Claim 2 has been amended to define an abbreviation. Support for this amendment is found in the specification at col. 1, line 28. Claim 12 has been amended to ensure correct antecedent basis. Support for this amendment is found in claim 4 as originally filed. Thus, no new matter is added by these amendments.

For the Examiner's convenience, a clean copy of the amended claims is provided in Appendix A. All of the pending claims are provided in Appendix B for the Examiner's convenience.

Objections to the Specification Under 35 U.S.C. § 132

The amendment filed March 1, 2002 is objected to as allegedly containing new matter. The Examiner alleges that there is no disclosure of "intact herpes virion" in the original disclosure. Applicants respectfully assert that the specification supports a recitation of intact herpes virions. For example, column 7, lines 16-23 describe the propagation of herpes virions. In particular, col. 7, lines 33-34 explicitly describe visual identification of "highly enriched virions with very little cellular debris." Accordingly, Applicants respectfully request withdrawal of this objection.

Request for Corrected Priority Information

Correction of the priority information is requested. In particular, the Examiner points out that the filing date of parent application 07/228,550 is incorrectly listed as August 4, 1998 and that reissue information and U.S. Patent No. 6,043,283 (the '283 patent) should be added. The priority information has been updated to correct the typographical error and to add the reissue information.

Applicants also respectfully note one basis for filing the present reissue application was to correct the '283 patent's failure to adequately claim priority under 35 U.S.C. § 120 to an earlier filed copending U.S. Patent application.

As explained in paragraph 7 of the reissue declaration by the patentees, the specification correctly states that the application from which U.S. Patent No. 6.054,283 issued is a divisional of USSN 08/392,674, filed February 22, 1995 which was a continuation of USSN 07/754,220, filed August 27, 1991, which was a continuation of USSN 07/255,712, filed October 11, 1988, which was a CIP of USSN 07/228,550, filed August 4, 1988, which was a CIP of USSN 06/901,602, filed August 29, 1986, which was a CIP of USSN 06/892,423, filed August 4, 1986. However, the specification

incorrectly states that USSN 06/892,423 was a CIP of USSN 06/895,857, filed August 12, 1986, which was a CIP of USSN 06/895,463, filed August 11, 1986. USSN 06/892,423, USSN 06/895,857, and USSN 06/895,463 were in fact not CIP's of each other.

Accordingly, Applicants respectfully request correction of the priority information and withdrawal of this objection.

Surrender of Original Patent

The Examiner states that the original patent or a statement as to its loss or inaccessibility must be received before the reissue application can be allowed. Applicants will surrender the patent to overcome this objection after the Examiner determines that the pending claims are otherwise allowable.

Oath/Declaration

The reissue declaration by the patentees is objected to as defective because it allegedly does not state that the person making the declaration acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 C.F.R. 1.56. Applicants respectfully point to paragraph 6 of the reissue declarations which explicitly states that:

> We acknowledge the duty to disclose information of which we are aware and which is material to the examination of this application for reissue of the original Letters Patent in accordance with 37 C.F.R. § 1.56.

In addition, during the telephonic discussion with Examiner Salmini on January 13, 2003 regarding the reissue declaration, Examiner Salimi noted that the reissue declaration should state that the errors in the patent arose without deceptive intent on the part of the Applicant. Applicants pointed to paragraphs 8 and 10 which contain explicit statements that "errors [regarding the priority information] arose without any

deceptive intent on our part" and "errors in claiming less than we had a right to claim arose without any deceptive intention on our part."

Examiner Salimi agreed that the language of the of the declaration is acceptable to show that the errors were made without any deceptive intent. Accordingly, Applicants respectfully request withdrawal of this objection.

Information Disclosure Statement

The Office Action states that Applicants have not furnished the Office with a list of all the references cited during the prosecution of U.S. Patent No. 6,054,283. An Information Disclosure Statement listing all of the references cited during the prosecution of U.S. Patent No. 6,054,283 accompanies this Amendment. Accordingly, Applicants respectfully request withdrawal of this objection.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-2 and 4-12 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection. In the instant case, the specification adequately defines the terms or the terms are adequately understood to one of skill in the art, such that the claims are not indefinite under 35 U.S.C. §112, second paragraph. Several bases of indefiniteness were raised, and they will be discussed in turn.

a. Claim 1

Claim 1 is allegedly unclear because according to the Examiner the claimed antibodies read on antibodies that bind to all herpes virus. Claim 1 explicitly recites that the antibodies bind to a herpes virus with genomic DNA that hybridizes to the nucleic acid of molecular clone ZVH14 (ATCC Accession No. 40,247), not to all herpes viruses. In addition, claim 1 specifically excludes antibodies which specifically bind to antigenic molecules from Epstein-Barr virus, human cytomegalovirus (CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri. Thus, one of skill in the art would easily determine the scope of claim 1 and would appreciate that

claim 1 is not directed to antibodies that bind to all herpes viruses. Accordingly, Applicants respectfully request that the rejection be withdrawn.

b. Claim 2

Claim 2 is allegedly unclear because the intended antibodies are not defined. Claim 2 is dependent on claim 1. Dependent claims incorporate all of the elements of the claim on which they depend. Therefore, claim 2 is directed to antibodies which specifically bind to an antigenic molecule from an isolated human herpes virus wherein the genomic DNA from the herpes virus binds to the nucleic acid of molecular clone ZVK14. In addition, through its dependence on claim 1, claim 2 specifically excludes antibodies which specifically bind to antigenic molecules from Epstein-Barr virus, human cytomegalovirus (CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri. Thus, one of skill in the art would easily determine the scope of claim 2. Accordingly, Applicants respectfully request that the rejection be withdrawn.

c. Claim 4

Claim 4 is allegedly unclear as the intended "human herpes virus antigen" is not defined. As suggested by the Examiner, Applicants have amended the claim to clarify that one characteristic of the intended virus lies in the fact that its genomic DNA hybridizes under stringent conditions to nucleic acid of molecular clone ZVH14 (ATCC Accession No. 40,247). Accordingly, Applicants respectfully request that this aspect of the rejection be withdrawn.

d. Claim 12

Claim 12 is allegedly unclear because of the recitation of "human herpes virus present on an intact herpes virion." For clarity, claim 12 has been amended to recite that the "human herpes virus antigen is present on an intact herpes virion." Accordingly, Applicants respectfully request that this aspect of the rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1, 2, and 4-12 are rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled and as allegedly lacking written description. Applicants respectfully traverse these rejections.

The present invention is a new HBLV (HHV-6) virus and variants thereof. The invention has opened the door to compositions and methods for studying herpes viruses. However, as explicitly set forth in the claims, the invention does not encompass every class of herpes viruses.

Enablement

In making the rejection, the Examiner states that the claims are enabled for an isolated antibody directed against the capsid glycoproteins of a HHV-6 virus identified as ATCC Accession No. 40,247 and methods of utilizing the capsid antigens in diagnostic methods for detecting the presence of antibodies against the HHV-6 virus, but alleges that the claims are not enabled for antibodies against all HHV-6 types or antibodies against all herpes viruses.

A particular claim is enabled by the disclosure in an application if the disclosure, at the time of filing, contains sufficient information so as to enable one of skill in the art to make and use the claimed invention without undue experimentation (*see, e.g., In re Wands*, 8 USPQ2d, 1400 (Fed. Cir. 1988), or MPEP §2164.01). A rejection for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments" (*see,* MPEP § 2164.08).

The present claims are directed to antibodies which specifically bind to an antigenic molecule of an isolated human herpes virus-6 (HHV-6), wherein the genomic DNA from the HHV-6 hybridizes to the nucleic acid of molecular clone ZVH14 (ATCC Accession No. 40,247) and methods of detecting such antibodies in a biological sample. The isolated HHV-6 recited in the claims has the morphology of a human herpes virus and a double-stranded DNA genome of about 170 Kb. The claimed antibodies do not specifically bind to antigenic molecules from Epstein-Barr virus, human cytomegalovirus

(CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri.

The claims do not encompass antibodies against all HHV-6 types nor do the claims encompass antibodies against all herpes viruses. The claims are directed only to antibodies which specifically bind to antigenic molecules of the isolated HHV-6 set forth in the claims. Applicants respectfully assert that based on the claims and specification, one of skill in the art could identify antibodies and diagnostic methods embraced by the breadth of the claims. Both the specification and claims provide a detailed description of the distinguishing aspects of the morphology and genome of the particular HHV-6 virus recited in the claims. For example, the claims require that the HHV-6 antigens to which the antibodies bind be from an HHV-6 virus with genomic DNA that hybridizes to the nucleic acid of molecular clone ZVH14. The claims also explicitly recite that the isolated HHV-6 virus has a double stranded DNA genome of about 170 Kb. In addition, the specification describes HHV-6 as new virus and teaches that HHV-6 lacks immunologic, antigenic, and genomic relatedness when compared to other known human herpesviruses (*see, e.g.*, col. 1, lines 51-55, col. 6, lines 3-16, and Tables 2 and 3). Therefore, antibodies that bind to all herpes viruses are not encompassed by the claims. The claims are directly only to antibodies that specifically bind to a particular HHV-6 virus that is amply described in both the specification and claims of the present application. Thus, there is ample guidance in the specification and claims for one of skill in the art to identify the claimed antibodies directed against the particular HHV-6 recited in the claims without undue experimentation.

In view of the foregoing remarks, Applicants respectfully assert that enablement has been satisfied for claims 1, 2, and 4-12 by the teachings in the specification and request withdrawal of this rejection.

Written Description

In making this rejection, the Examiner states that the claims are drawn to a multitude of antibodies and antigens and alleges that applicants are entitled only to

antibodies against the capsid proteins of the deposited virus identified by ATCC Accession No. 40,247.

Applicants respectfully traverse this rejection and submit that all of the claims as presently pending are adequately described in the specification. As set forth in MPEP §2163 IIA3(a), "[a]n adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize the inventor has possession of the claimed invention," citing *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323, 56 USPQ 2d 1481,1483 (Fed. Cir. 2000). MPEP §2163 IIA3(a) further states that identifying characteristics for biomolecules (*e.g.*, antibodies) include binding specificity. Moreover, as set forth in the Example 16 of the Written Description Guidelines Training Materials, the 35 U.S.C. § 112, first paragraph written description requirement is satisfied for a claimed antibody if the specification teaches that an antigen has been isolated and is useful for detection of viral infection.

As explained above, the present claims are directed to antibodies which *specifically bind* to an antigenic molecule from an isolated human herpes virus-6 (HHV-6), wherein the genomic DNA from the HHV-6 hybridizes to the nucleic acid of molecular clone ZVH14 (ATCC Accession No. 40,247). As explicitly recited in the claims, the antibodies do ***not*** specifically bind to antigenic molecules from Epstein-Barr virus, human cytomegalovirus (CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri.

The claims and specification provide ample guidance regarding the binding specificity of the claimed antibodies by clearly describing the isolated HHV-6 virus which is the source of the antigens to which the claimed antibodies specifically bind. For example, the claims require that the isolated HHV-6 virus have genomic DNA that hybridizes to the nucleic acid of molecular clone ZVH14. As set forth in the specification ZVH14 can be used as a probe to definitively detect the presence of HBLV (*i.e.*, the particular HHV-6 recited in the claims) (*see, e.g.*, col. 5, lines 18-22). In addition, both the specification and claims provide a detailed description of the

distinguishing aspects of the morphology and genome of the particular HHV-6 virus recited in the claims and provides data illustrating the differences between this HHV-6 and other herpes viruses. For example, the specification explicitly states that HHV-6 lacks immunologic, antigenic, and genomic relatedness when compared to other known human herpesviruses (*see, e.g.*, col. 1, lines 51-55, col. 6, lines 3-16, and Tables 2 and 3). Finally, the claims and specification explicitly state that claimed antibodies do not specifically bind to antigenic molecules from other herpes viruses, *e.g.*, Epstein-Barr virus, human cytomegalovirus (CMV), Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri. Thus, one of skill in the art would be able to identify the antibodies that specifically bind to antigens from the particular HHV-6 virus recited in the claims.

The claimed antibodies, however, are not limited to those which specifically bind the capsid antigens of the HHV-6. The specification describes multiple HHV-6 antigenic proteins, teaches that they may be isolated using standard purification techniques known in the art, and teaches that reactions between these HHV-6 antigenic proteins and antibodies that specifically bind to them may be detected using standard techniques known in the art. More specifically, the specification describes immunoassay detection of *multiple* HHV-6 antigens, including HHV-6 capsid antigens (col. 6, lines 17-43), HHV-6 viral membrane antigens (col. 6, lines 44-53 and Fig. 2), and several other HHV-6 proteins (col. 10, lines 27-48 and Figures 6, 14, and 15). Thus, the specification provides ample explicit support for antibodies that recognize multiple antigenic proteins of the particular HHV-6 recited in the claims and the present invention is not limited to antibodies against only the capsid proteins of such an HHV-6. Therefore, because the specification teaches the isolation of multiple HHV-6 antigens and further teaches that their interaction with antibodies may be detected, the presently claimed invention meets the written description guidelines discussed above.

In view of the foregoing remarks, Applicants respectfully assert that written description has been satisfied for claims 1, 2, and 4-12 by the teachings in the specification and request withdrawal of this rejection.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 2, and 4-12 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Middeldorp *et al., J. Clin. Microbiol.*, (1984) 20(4); 763-771, in view of and further substantiated by Lawrence *et al., J. Virol.* (1990) 287-289. Applicants respectfully traverse this rejection.

For a rejection of claims under § 102(b) to be properly founded, the cited reference must disclose ***all*** of the elements, features or limitations of the claimed invention. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

The present invention is directed to antibodies which specifically bind to an antigenic molecule from an isolated human herpes virus, but not to an antigenic molecules from Epstein-Barr virus, *human cytomegalovirus (CMV)*, Herpes Simplex virus (HSV), Varicella-Zoster virus (VZV), or Herpes virus saimiri; and methods of detecting such antibodies in a biological sample.

Middeldorp *et al.* is cited as disclosing antibodies against CMV antigens and methods of using the antibodies to detect the presence of CMV antigens. Lawrence *et al.* is cited for disclosing that CMV and HHV-6 are closely related viruses that share similar antigens.

Middeldorp *et al.* describe an immunoassay for detection of immunoglobulin M and antibodies with specificity for human cytomegalovirus (CMV) early (CMV-EA) and late (CMV-LA) antigens. Middeldorp *et al.* contains no disclosure of human herpesvirus-6 (HHV-6), of antibodies that specifically bind HHV-6, or of methods of detecting HHV-6 using such antibodies. Lawerence *et al.* describes a comparison of the sequences of HHV-6 and CMV and discloses that based on their sequences, HHV-6 and CMV are closely related. However, Lawrence *et al.* is devoid of any disclosure regarding antibodies that specifically bind to antigenic molecules from ***either*** virus and, in contrast to the presently claimed invention, does not contain any disclosure of antibodies that specifically bind to antigenic molecules from HHV-6, but ***not*** to antigenic molecules from CMV.

Therefore, the cited references do not disclose all of the elements of the claimed invention. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(a)

Claims 1, 2, and 4-12 are rejected under 35 U.S.C. § 102(a) as allegedly anticipated by Rodgers *et al.*, *J. Gen. Virol.* (1985), 66:2045-2049, in view of and further substantiated by Lawrence *et al.*, *J. Virol.* (1990) 287-289. Applicants respectfully traverse this rejection.

For a rejection of claims under § 102(a) to be properly founded, the cited reference must disclose ***all*** of the elements, features or limitations of the presently claimed invention. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987).

As explained above, the present invention is directed to antibodies which specifically bind to an antigenic molecule from an isolated human herpes virus, but not to an antigenic molecules from, *inter alia, human cytomegalovirus (CMV)*; and methods of detecting such antibodies in a biological sample.

Rodgers *et al.* is cited as disclosing specific antibodies against CMV and methods of using the antibodies in assays to detect CMV antigens. Lawrence *et al.* is cited for disclosing that CMV and HHV-6 are closely related viruses that share similar antigens.

Rodgers *et al.* describe the characteristics of four monoclonal antibodies specific for human cytomegalovirus (CMV) early (CMV-EA) and late (CMV-LA) antigens. Rodgers *et al.* contains no disclosure of human herpesvirus-6 (HHV-6), of antibodies that specifically bind HHV-6, or of methods of detecting HHV-6 using such antibodies. As explained above, in contrast to the presently claimed invention, Lawrence *et al.* does not contain any disclosure of antibodies that specifically bind to antigenic molecules from HHV-6, but ***not*** to antigenic molecules from CMV.

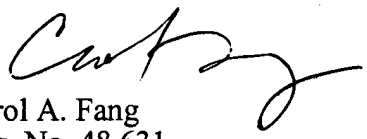
Thus, the cited references fail to disclose all of the elements of the claimed invention and do not anticipate the claimed invention. Therefore, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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